# CENTER FOR DRUG EVALUATION AND RESEARCH

## APPLICATION NUMBER _____

## ADMINISTRATIVE DOCUMENTS

# REVIEW OF PROFESSIONAL LABELING
# DIVISION OF LABELING AND PROGRAM SUPPORT
# LABELING REVIEW BRANCH

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**Date of Review: June 6, 1996 Date of Submission: Nov. 3, 1995**

**Primary Reviewer: Charlie Hoppes**

**Secondary Reviewer: Adolph Vezza**

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**ANDA Number: 74-707 Review Cycle: 1**

**Applicant's Name [as seen on 356(h)]: Circa Pharmaceuticals Inc.**

**Established Name: Nicotine Polacrilex Gum USP, 4 mg**

**LABELING DEFICIENCIES, WHICH ARE TO BE INCORPORATED WITH THE CHEMISTRY COMMENTS TO THE FIRM:**

[NOTE: These deficiencies can be located on the x-drive as detailed in notes from Ted Sherwood regarding the New X-Drive]

A. CHEMISTRY DEFICIENCIES

B. LABELING DEFICIENCIES

1. GENERAL COMMENTS:

   a. Please submit draft OTC labeling to this application.

   b. We encourage the inclusion of "USP" in the established name for this drug product where it appears on your labels and labeling.

2. CONTAINER

   a. See GENERAL COMMENTS.

   b. The innovator is required to market this product in a child-resistant blister. Please provide information regarding the child-resistant nature of your container.

3. CARTON

   We encourage the use of boxing, contrasting colors, or other means to differentiate the strengths of this

product from your proposed 2 mg strength product (ANDA

Please revise your labels and labeling, as instructed above, and submit draft labeling reflecting a change to OTC status.

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with the labeling of the listed drug with all differences annotated and explained.

Please note that we reserve the right to request further changes in your labels and/or labeling based upon further changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

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**APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):**

Do you have 12 Final Printed Labels and Labeling? Yes No
If no, list why:

Container Labels:

Carton Labeling:

Unit Dose Blister Label:

Unit Dose Carton Label:

Professional Package Insert Labeling:

Patient Package Insert Labeling:

Auxiliary Labeling:

Revisions needed post-approval:

BASIS OF APPROVAL:

Was this approval based upon a petition? Yes No

What is the RLD on the 356(h) form:

NDA Number:

NDA Drug Name:

NDA Firm:

Date of Approval of NDA Insert and supplement #:

Has this been verified by the MIS system for the NDA?
Yes No

Was this approval based upon an OGD labeling guidance?
Yes No

If yes, give date of labeling guidance:

Basis of Approval for the Container Labels:

Basis of Approval for the Carton Labeling:

Other Comments:

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# REVIEW OF PROFESSIONAL LABELING CHECK LIST

| Applicant's Established Name | Yes | No | N.A. |
|---|---|---|---|
| Different name than on acceptance to file letter? | X | | |
| Is this product a USP item? If so, USP supplement in which verification was assured. | X | | |
| Is this name different than that used in the Orange Book? | X | | |
| If not USP, has the product name been proposed in the PF? | | | X |
| **Error Prevention Analysis** | | | |
| *PROPRIETARY NAME* | | | |
| Has the firm proposed a proprietary name? If yes, complete this subsection. | | X | |
| Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present? | | | |
| Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified? | | | |
| *PACKAGING* -See applicant's packaging configuration in FTR | | | |
| Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR. | | X | |
| Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC. | | x | |
| Does the package proposed have any safety and/or regulatory concerns? | | X | |
| If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection? | | | x |
| Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration? | | x | |
| Is the strength and/or concentration of the product unsupported by the insert labeling? | | x | |

| | | | |
|---|---|---|---|
| Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect? | | x | |
| Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product? | x | | |
| Are there any other safety concerns? | | x | |
| *LABELING* | | | |
| Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label). | x | | |
| Has applicant failed to clearly differentiate multiple product strengths? | x | | |
| Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines) | | x | |
| **Error Prevention Analysis:** *LABELING* (Continued) | **Yes** | **No** | **N.A.** |
| Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA) | | x | |
| Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed? | | x | |
| Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED? | | | x |
| Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported. | | x | |
| **Scoring:** Describe scoring configuration of RLD and applicant (page #) in the FTR | | | |
| Is the scoring configuration different than the RLD? | | | x |
| Has the firm failed to describe the scoring in the HOW SUPPLIED section? | | | x |
| **Inactive Ingredients:** (FTR: List page # in application where inactives are listed) | | | |
| Does the product contain alcohol? If so, has the accuracy of the statement been confirmed? | | x | |
| Do any of the inactives differ in concentration for this route of administration? | | x | |
| Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)? | | x | |
| Is there a discrepancy in inactives between DESCRIPTION and the composition statement? | | x | |
| Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported? | | x | |
| Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray? | | x | |
| Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION? | | x | |
| Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed) | | x | |
| **USP Issues:** (FTR: List USP/NDA/ANDA dispensing/storage recommendations) | | | |

| | | | |
|---|---|---|---|
| Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable? | | x | |
| Does USP have labeling recommendations? If any, does ANDA meet them? | | x | |
| Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container? | | x | |
| Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling. | | x | |
| **Bioequivalence Issues:** (Compare bioeqivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable) | | | |
| Insert labeling references a food effect or a no-effect? If so, was a food study done? | | x | |
| Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why. | | | x |
| **Patent/Exclusivity Issues:** FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state. | | | |

**FOR THE RECORD:**

1. **Container labels, carton and User's Guide labeling were reviewed against the labeling of Nicorette®, NDA 20-066/S-004, approved February 9, 1996.**

2. **This is a first generic product.**

3. **No patents or exclusivities are listed in the 16th edition of the Orange Book or in Supplement 3 to the 16th ed. for nicotine polacrilex gum. Supp 3 shows that the Rx versions of this product have been deleted.**

4. **This is a USP item. The monograph appears in the 1st supplement to USP 23.**

5. **The applicant has submitted OTC labeling to the sister application ANDA mg) and has requested a change in status from Rx to OTC. we have requested that the firm submit draft OTC labeling to this application as well. See FTR in review for for a discussion of issues regarding the OTC labeling.**

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Primary Reviewer

6/6/96

Date

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Acting Team Leader,
Labeling Rev. Branch

6/6/96

Date

cc:
ANDA 74-707
HFD-613\CHoppes\AVezza\no cc:
njg/6/6/96/x:/.../74707na1.l
Review

## DIVISION APPROVAL SUMMARY

**ANDA #:** 74-707 **DRUG PRODUCT:** Nicotine Polacrilex Gum 4 mg, USP

**FIRM:** Circa Pharmaceuticals, Inc.

**DOSAGE:** Chewing Gum

**STRENGTH:** 4 mg/piece

**cGMP STATEMENT/EIR UPDATE STATUS:**
cGMP: GMP Certification is enclosed. (Page 696).
EER: FUR Status pending.

**BIO STUDY(ies)/BIOEQUIVALENCE STATUS:**
A `no further comments' letter has been issued to the firm after the chew-out study review was completed.

**METHODS VALIDATION** (Including dosage form description):
N/A. Drug substance and drug product are compendial. However, for the 2 mg Gum, methods validation was completed and found satisfactory.

**STABILITY**(Conditions, Containers, methods):
Bio batch

**Evaluation of stability indicating methods:**

**Stability Assays**

| Tests | Method | Specification |
|---|---|---|
| Description | | off white color. |
| Blister packaging Assay | | |
| Chro.Purity* | | |
| Blister seal Integrity | | |

Stability studies were done on the bio batch. Packaging configurations (blister packs) are the same those listed in the container section. Stability studies are in conformance with the FDA Guidelines.

**LABELING REVIEW STATUS:** Satisfactory dated 11/25/98.

**STERILIZATION VALIDATION** (If Applicable): Not applicable for this product.

**BATCH SIZES:**

**BIO BATCH:** Lot RD#1201 and RD1202
NDS source: The Nicobrand Company

**STABILITY BATCHES** (different from BIO BATCH, manuf. site, process)
Stability batch is the same as the bio-batch

**PROPOSED PRODUCTION BATCH**
is the proposed production batch size.

Process is the same as the demonstration batch. Reprocessing statement is provided in volume 2.1 (under Attachment 1).

**COMMENTS:** Approvable

**CHEMISTRY REVIEWER:** **DATE:**

Radhika Rajagopalan /S/ January 11, 1999 1/21/99

cc: ANDA 74-707

Endorsements:
HFD-645/RRajagopalan/1/11/99 /S/ 1/21/99
HFD-645/BTArnwine/1/20/99 (3) pneumine 1/21/99

F/T by pah/1/21/99
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PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

| TO (Division/Office) | | FROM: | |
|---|---|---|---|
| HFD-170 DIVISION OF ANESTHETIC, CRITICAL CARE | | OFFICE OF GENERIC DRUGS | |
| DATE | IND NO. | NDA NO. | TYPE OF DOCUMENT | DATE OF DOCUMENT |
| 3/6/96 | | 74-707 | ORIGINAL ANDA | 6/6/95 + 11/3/9 |
| NAME OF DRUG | | PRIORITY CONSIDERATION | CLASSIFICATION OF DRUG | DESIRED COMPLETION DA |
| NICOTINE POLACRILEX GUM | | | | 5/8/96 |

NAME OF FIRM
CIRA PHARMACEUTICALS, INC.

## REASON FOR REQUEST

### I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY _____
- ☐ PRE-NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☒ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ OTHER *(Specify below)*

### II. BIOMETRICS

| STATISTICAL EVALUATION BRANCH | STATISTICAL APPLICATION BRANCH |
|---|---|
| ☐ TYPE A OR B NDA REVIEW | ☐ CHEMISTRY |
| ☐ END OF PHASE II MEETING | ☐ PHARMACOLOGY |
| ☐ CONTROLLED STUDIES | ☐ BIOPHARMACEUTICS |
| ☐ PROTOCOL REVIEW | ☐ OTHER |
| ☐ OTHER | |

### III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILITY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL– BIOPHARMACEUTICS
- ☐ IN–VIVO WAIVER REQUEST

### IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS *(List below)*
- ☐ COMPARATIVE RISK ASSESSEMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAF
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

### V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS *(Attach additional sheets if necessary)*

ATTENTION: MARY LAMBERT, CSO
PLEASE EVALUATE THE SAFETY OF THE INACTIVE INGREDIENT, THAT IS CONTAINED IN THE PROPOSED DRUG PRODUCT. ALTHOUGH THE INACTIVE INGREDIENT IS ACCEPTED FOR USE IN CERTAIN FOOD PRODUCTS, IT HAS NOT BEEN PREVIOUSLY APPROVED IN A DRUG PRODUCT.

PLEASE RETURN THE COMPLETED CONSULT AND THE DOCUMENT TO:
OFFICE OF GENERIC DRUGS - HFD 600
DOCUMENT CONTROL ROOM
ROOM 150
METRO PARK NORTH II

THANK YOU

| SIGNATURE OF REQUESTER | METHOD OF DELIVERY *(Check one)* |
|---|---|
| CECELIA PARISE, CSO, HFD-615 594-0315 | ☒ MAIL ☐ HAND |
| SIGNATURE OF RECEIVER | SIGNATURE OF DELIVERER |

FORM FDA 3291 (7/83)

SEND THROUGH HFD-103 ATTN EDWINA UNDERWOOD 15045

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**
**PUBLIC HEALTH SERVICE**
**FOOD AND DRUG ADMINISTRATION**

# REQUEST FOR CONSULTATION

ALL

| TO (Division/Office) | | | FROM: | |
|---|---|---|---|---|
| HFD-170 DIVISION OF ANESTHETIC, CRITICAL CARE | | | OFFICE OF GENERIC DRUGS | |
| DATE 3/6/96 | IND NO. | NDA NO. 74-707 | TYPE OF DOCUMENT ORIGINAL ANDA | DATE OF DOCUMENT 6/6/95 + 11/3/95 |
| NAME OF DRUG NICOTINE POLACRILEX GUM | | PRIORITY CONSIDERATION | CLASSIFICATION OF DRUG | DESIRED COMPLETION DATE 5/8/96 |

NAME OF FIRM
CIRA PHARMACEUTICALS, INC.

## REASON FOR REQUEST

### I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY _____
- ☐ PRE-NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☒ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ OTHER *(Specify below)*

### II. BIOMETRICS

| STATISTICAL EVALUATION BRANCH | STATISTICAL APPLICATION BRANCH |
|---|---|
| ☐ TYPE A OR B NDA REVIEW | ☐ CHEMISTRY |
| ☐ END OF PHASE II MEETING | ☐ PHARMACOLOGY |
| ☐ CONTROLLED STUDIES | ☐ BIOPHARMACEUTICS |
| ☐ PROTOCOL REVIEW | ☐ OTHER |
| ☐ OTHER | |

### III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILITY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL– BIOPHARMACEUTICS
- ☐ IN–VIVO WAIVER REQUEST

### IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS *(List below)*
- ☐ COMPARATIVE RISK ASSESSEMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

### V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS *(Attach additional sheets if necessary)*

ATTENTION: MARY LAMBERT, CSO
PLEASE EVALUATE THE SAFETY OF THE INACTIVE INGREDIENT, [redacted] THAT IS CONTAINED IN THE PROPOSED DRUG PRODUCT. ALTHOUGH THE INACTIVE INGREDIENT IS ACCEPTED FOR USE IN CERTAIN FOOD PRODUCTS, IT HAS NOT BEEN PREVIOUSLY APPROVED IN A DRUG PRODUCT.

PLEASE RETURN THE COMPLETED CONSULT AND THE DOCUMENT TO:
OFFICE OF GENERIC DRUGS - HFD 600
DOCUMENT CONTROL ROOM
ROOM 150
METRO PARK NORTH II

THANK YOU

Review Complete /S/ 5-2-96

/S/ 4/96

SIGNATURE OF REQUESTER

ELIA PARISE, CSO, HFD-615 594-0315

METHOD OF DELIVERY *(Check one)*
☒ MAIL ☐ HAND

SIGNATURE OF RECEIVER

SIGNATURE OF DELIVERER

FORM FDA 3291 (7/83)

**TENTATIVE APPROVAL SUMMARY**

# REVIEW OF PROFESSIONAL LABELING
# DIVISION OF LABELING AND PROGRAM SUPPORT
# LABELING REVIEW BRANCH

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**ANDA Number: 74-707 Date of Submission: September 2, 1998**

**Applicant's Name: Circa Pharmaceuticals Inc.**

**Established Name: Nicotine Polacrilex Gum USP, 4 mg**

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**APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):**

Do you have 12 Final Printed Labels and Labeling? No. Draft labels and labeling are all that's needed for tentative approval.

Carton Labeling (Starter): 108s
*Satisfactory as of September 2, 1998 submission.*
Carton Labeling (Refill): 48s
*Satisfactory as of September 2, 1998 submission.*
Unit Dose Blister Label:
*Satisfactory as of September 2, 1998 submission.*
User's Guide:
*Satisfactory as of September 2, 1998 submission.*
Audio Tape:
*Satisfactory as of September 2, 1998 submission. - We are awaiting an opinion from the Office of General Counsel as to whether this is a labeling piece and whether it should be the "same as".*

Revisions needed before full approval: Firm must include the toll-free telephone number. See firm's comments in the September 9, 1998 letter.

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Nicorette® Gum

NDA Number: 20-066

NDA Drug Name: Nicorette® (Nicotine Polacrilex) Gum

NDA Firm: SmithKline Beecham

Date of Approval of NDA Insert and supplement #: 2/9/96 (S-004)
Has this been verified by the MIS system for the NDA? S-004 is not in the MIS system.

Was this approval based upon an OGD labeling guidance? No

Basis of Approval for the Unit Dose Blister Labels: labels on file

Basis of Approval for the Carton Labeling: labeling on file

Basis of Approval for the User's Guide: labeling on file

Basis of Approval for the Audio Tape: script of tape on file

Other Comments:

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# REVIEW OF PROFESSIONAL LABELING CHECK LIST

| Applicant's Established Name | Yes | No | N.A. |
|---|---|---|---|
| Different name than on acceptance to file letter? | X | | |
| Is this product a USP item? If so, USP supplement in which verification was assured. | X | | |
| Is this name different than that used in the Orange Book? | X | | |
| **Error Prevention Analysis** | | | |
| *PROPRIETARY NAME - None proposed* | | X | |
| *PACKAGING* -See applicant's packaging configuration in FTR | | | |
| Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR. | | X | |
| Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC. | | X | |
| Does the package proposed have any safety and/or regulatory concerns? | | X | |
| Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration? | | X | |
| Is the strength and/or concentration of the product unsupported by the insert labeling? | | X | |
| Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect? | | X | |
| Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product? | X | | |

| | | | |
|---|---|---|---|
| Are there any other safety concerns? | | x | |
| *LABELING* | | | |
| Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label). | x | | |
| Has applicant failed to clearly differentiate multiple product strengths? | x | | |
| Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines) | | x | |
| **Error Prevention Analysis:** *LABELING* (Continued) | **Yes** | **No** | **N.A.** |
| Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA) | | x | |
| Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed? | | x | |
| Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED? | | | x |
| Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported. | | x | |
| **Inactive Ingredients:** (FTR: List page # in application where inactives are listed) | | | |
| Does the product contain alcohol? If so, has the accuracy of the statement been confirmed? | | x | |
| Do any of the inactives differ in concentration for this route of administration? | | x | |
| Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)? | | x | |
| Is there a discrepancy in inactives between DESCRIPTION and the composition statement? | | x | |
| Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported? | | x | |
| Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray? | | x | |
| Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed) | | x | |
| **USP Issues:** (FTR: List USP/NDA/ANDA dispensing/storage recommendations) | | | |
| Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable? | | x | |
| Does USP have labeling recommendations? If any, does ANDA meet them? | | x | |
| Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container? | | x | |
| Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling. | | x | |
| **Bioequivalence Issues:** (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable) | | | |
| Insert labeling references a food effect or a no-effect? If so, was a food study done? | | x | |
| Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why. | | | x |
| **Patent/Exclusivity Issues:** FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state. | | | |

FOR THE RECORD: (portions taken from previous review)

1. Container labels, carton and User's Guide labeling were reviewed against the labeling of Nicorette®, NDA 20-066/S-004, approved February 9, 1996.

2. This is a first generic product.

3. There is a new product exclusivity for the OTC drug product listed in the 17th edition of the Orange Book which expires February 9, 1999. The Rx versions of this product have been deleted.

4. This is a USP item. The monograph appears in the 1st supplement to USP 23.

5. See FTR in review for for a discussion of issues regarding the OTC labeling.

6. The firm has revised their flavoring to more closely match that of the reference listed drug.

   The firm has submitted a double blind study (found in Attachment 15 - Volume 2.2) to determine preference of proposed gum vs. Nicorette®. The findings were that:
   - Neither product was perceived as "tasting good".
   - The applicant's gum "was perceived as less favorable or equivalent to Nicorette®.

   Dr. Fanning has looked at this study and found it satisfactory.

7. The bio has been found acceptable; the applicant reformulated the product using ycerin and a bio waiver was granted.

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Date of Review: 11-25-98 Date of Submission: 9-2-98

Primary Reviewer: Adolph Vezza Date: 11/25/98

Team Leader: Charlie Hoppes Date 11/25/98

/S/ 11/25/98

S&REV\74707TAP.L

RECORD OF TELEPHONE CONVERSATION

I called Joyce DelGaudio of Circa regarding the addition of blister leak test for the 4 mg gum. In October, 98, Florence Fang, Acting Director had requested the same as an amendment to the 2 mg dosage. The firm did not include this earlier for the 4 mg product. She will provide this as a Telephone amendment.

1/28/99

**DATE**
1/28/99

**ANDA NUMBER**
74-707

**IND NUMBER**

**TELECON**

**INITIATED BY** _ APPLICANT/ SPONSOR X FDA

**MADE** X BY TELE. _ IN PERSON

**PRODUCT NAME**
Nicotine Polacrilex Gum 4 mg

**FIRM NAME**
Circa

**NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD**
Joyce DelGaudio

**TELEPHONE NUMBER**
516-842-8383

**SIGNATURE**
Radhika Rajagopalan